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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of: Mathur, et al.

Serial No.: 09/707,121 Group Art Unit: 1652

Filed: November 6, 2000 Examiner: Y. Pak

For: NOVEL HUMAN KINASE PROTEIN AND POLYNUCLEOTIDES ENCODING THE SAME

Attorney Docket No.: LEX-0083-USA

REQUEST FOR CONTINUED EXAMINATION UNDER 37 C.F.R. § 1.114
AMENDMENT AND RESPONSE

Commissioner for Patents
Washington, D.C. 20231

Sir:

The Applicants acknowledge the receipt of the Advisory Action mailed on March 08, 2002 (Paper No. 13), which has been carefully reviewed and studied. The Applicants respectfully request continued examination of application Serial No: 09/707,121 and submit the following amendment and respectfully request reconsideration of the application in view of this amendment and remarks. Applicants hereby authorize Commissioner to withdraw the fee due under 37 C.F.R. 1.17(e) to Deposit Account No. 50-0892. Applicants believe that this request for continued examination is therefore complete and filed in a timely manner and that no additional fee is due in connection with this

response. However, the Commissioner is authorized to charge any underpayment or credit any overpayment to Deposit Account No. 50-0892.

AMENDMENTS

A clean copy of the pending and amended claims are attached as Exhibit A. A marked up copy of the pending claims are attached as Exhibit B.

Please amend Claim 2 so that the text of the amended claim reads as follows, such that highly stringent hybridization conditions include the washing conditions (which determine stringency) that are described verbatim in the specification.

2. (Twice Amended) An isolated nucleic acid molecule comprising a novel human kinase nucleotide sequence that:

(a) encodes the amino acid sequence shown in SEQ ID NO: 2; and

(b) hybridizes under highly stringent conditions to the nucleotide sequence of SEQ ID NO: 1 or the full complement thereof, wherein highly stringent conditions include washing in 0.1xSSC/0.1% SDS at 68°C.

I. Status of Claims

Claims 2-4 are pending in the instant application. With this amendment Claims 2 is amended. For the convenience of the Examiner, a clean copy of the pending claims is attached hereto as **Exhibit**

A. In compliance with 37 C.F.R. § 1.121(c)(1)(ii), a marked up copy of the original claims is attached hereto as **Exhibit B**.

II. Support for the New Claims

Amendment of Claim 2 finds support throughout the specification as originally filed, with particular support for the specific highly stringent hybridization condition being found at least at page 4, lines 19. As the amendment to Claim 2 is fully supported by the specification and claims as originally filed, it does not constitute new matter. Entry therefore is respectfully requested.

RESPONSE

III. Rejections Under 35 U.S.C. § 101

Claims 2-4 stand rejected under 35 USC section 101, as being allegedly not supported by a specific and substantial utility or a well-established utility. The Examiner's rejection is respectfully traversed. As taught in the application and as well known to those of skill in the art, kinase proteins play a critical role in, *intra alia*, signal transduction and cell activation. In fact, many oncogenes are kinases or kinase linked receptors. Kinases are also well known to the art as targets for compounds that inhibit cellular signaling and regulation. Many highly successful and highly profitable drug therapies are directed at kinases. Therapies directed at human kinases include, among others, many of those for cancer and several antiviral medications. Therefore, the identification of a new and novel human kinase has great utility.

Applicants have presented evidence of multiple utilities in previous responses dated October 5, 2001 and January 11, 2002, among these are that kinases are well known the art to be valuable drug targets. That U.S. Patents have been issued on kinase fragments (U.S. Patent No: 5,817,479) and that if novel kinase fragments have utility, logically novel full-length human kinases should also have utility. As a further example of the utility of the presently claimed polynucleotides, the Examiner is respectfully reminded that only a minor percentage of the genome actually encodes exons, which in-turn encode amino acid sequences. The presently claimed polynucleotide sequences of this novel human kinase provide biologically validated empirical data (*e.g.*, showing which sequences are transcribed, spliced, and polyadenylated) that *specifically* define that portion of the corresponding genomic locus that actually encodes exon sequence. Equally significant is that the claimed polynucleotide human kinase sequences define how the encoded exons are actually spliced together to produce an active transcript (*i.e.*, the described sequences are useful for functionally defining exon splice-junctions). The Applicants respectfully submit that the practical scientific value of expressed, spliced, and polyadenylated mRNA sequences is readily apparent to those skilled in the relevant biological and biochemical arts.

Given the legal test for utility simply involves an assessment of whether those skilled in the art would find any of the utilities described for the invention to be credible or believable, this is clear evidence that those skilled in the art would have recognized the function and activity of the kinase encoded by the sequences of the present invention, there can, therefore, be no question that Applicants' asserted utility for the described sequences is "credible." As such, the scientific evidence clearly establishes that Applicants have described an invention whose utility is in full compliance with the provisions of 35 U.S.C. § 101, and the Examiner's rejection should be withdrawn.

In addition, Applicants would like to further invite the Examiner's attention to the parts of the specification (Sections 5.0 and 5.1) that describe the use of sequences in a gene chip format to provide a high throughput analysis of the relevant cellular "transcriptome".

Evidence of the "real world" substantial utility of the present invention is provided by the fact that there is an entire industry established based on the use of gene sequences or fragments thereof in a gene chip format. Perhaps the most notable gene chip company is Affymetrix. However, there are many companies which have, at one time or another, concentrated on the use of gene sequences or fragments, in gene chip and non-gene chip formats, for example: Agilent Technologies, Gene Logic, ABI-Perkin-Elmer, HySeq and Incyte. In addition, one such company, Rosetta Inpharmatics, was viewed to have such "real world" value that it was acquired by large pharmaceutical company, Merck & Co., for substantial sums of money (net equity value of the transaction was $620 million). The "real world" substantial industrial utility of gene sequences or fragments would, therefore, appear to be widespread and well established. The sequences of the present invention describe a novel gene encoding a transporter and provide a unique identifier of the corresponding gene. Such gene chips clearly have utility, as evidenced by hundreds of issued U.S. Patents, such as U.S. Patent Nos. 5,445,934, 5,556,752, 5,744,305, 5,837,832, 6,156,501 and 6,261,776. The present nucleotide sequences encode a novel human kinase as detailed throughout the specification. Therefore, as the present sequences are specific markers of the human genome, and such specific markers are targets for the discovery of drugs that are associated with human disease, those of skill in the art would instantly recognize that the present nucleotide sequences would be an ideal, novel candidate for assessing gene expression using such gene chips.

The Examiner is further requested to consider that, given the huge expense of the drug discovery process, even negative information has great "real world" practical utility. Knowing that a given gene is not expressed in medically relevant tissue provides an informative finding of great value to industry by allowing for the more efficient deployment of expensive drug discovery resources. Such practical considerations are equally applicable to the scientific community in general, in the time and resources that are not wasted chasing what are essentially scientific dead-ends (from the perspective of medical relevance). Clearly, compositions that enhance the utility of such gene chips, such as the presently claimed nucleotide sequences, must in themselves be useful. Moreover, the presently described novel transporter provides uniquely specific sequence resources for identifying and quantifying full length transcripts that were encoded by the corresponding human genomic locus. Accordingly, there can be no question that the described sequences provide an exquisitely specific utility for analyzing gene expression.

Yet another example of the utility of the present invention is in expanding the utility of data coming from the human genome project. Persons of skill in the art, as well as thousands of venture capitalists and investors, readily recognize the utility, both scientific and commercial, of genomic data in general, and specifically human genomic data. All current therapeutics directly or indirectly interact with biological sequences encoded by the human genome, and virtually all future human therapeutics shall do likewise. Consequently, billions of dollars have been invested in the human genome project, resulting in useful genomic data (see, *e.g.*, Venter *et al.*, 2001, Science *291*:1304). The results have been a stunning success, as the utility of human genomic data has been widely recognized as a great gift to humanity (see, *e.g.*, Jasny and Kennedy, 2001, Science *291*:1153). Clearly, the usefulness of human

genomic data, such as the presently claimed nucleic acid molecules, is substantial and credible (worthy of billions of dollars and the creation of numerous companies focused on such information) and well-established (the utility of human genomic information has been clearly understood for many years).

As a further example of the utility of the presently claimed polynucleotides, the Examiner is respectfully reminded that only a minor percentage of the genome actually encodes exons that in-turn encode polypeptide sequences. The presently described kinase encoding cDNAs provide biologically validated empirical data (*e.g.*, showing which sequences are transcribed, spliced, and polyadenylated) that *specifically* define that portion of the corresponding genomic locus that actually encodes exon sequence. Equally significant is that the described cDNA sequences define which exons are actually spliced together to produce an active transcript (*i.e.*, such sequences are generally required to conclusively identify functional exon splice-junctions). The Applicants submit that one skilled in the art would have clearly understood that the above *substantial and specific* utilities as inherent features of the presently described sequences. Given the expression pattern of the kinase of the present invention in many major tissues, another utility for this novel human kinase would be as a target for life ending compounds. Such compounds include, but are not limited to, those used in euthanasia of the terminally ill or those condemned to receive capital punishment by the legal system.

The Examiner has questioned the identity of the novel human kinase of the present invention as a kinase. "Identifying a polynucleotide as encoding a kinase-like protein or proteinswith structural similarity to a particular enzyme does not endow the polynucleotide with such a utility." (Paper 13 at page 2) . In response, Applicants respectfully submit the following evidence strongly supporting the identity of the novel human kinase of the present invention as a kinase: (1) the protein of SEQ ID NO:2,

encoded by SEQ ID NO:1, clearly contains a protein kinase domain, as verified by protein structural analysis as accepted by those of skill in the art (InterPro and PFAM); (2) the sequence of SEQ ID NO:1 is 99% identical (2674/2682 nucleotides) to sequences of several PCT patent applications (WO 200210401 and WO 200166594), in which they these sequences are identified as kinases, thus clearly those of skill in the art recognize that the Applicants assertion that the novel human kinase of the present invention is indeed a kinase is credible.

In addition Applicants submit that previous amendment of the claims to include the phrase "novel human kinase" has rendered this rejection moot. Should Applicants stated assertion that the present invention encodes a novel human kinase be incorrect, the validity of the claims would certainly be challenged.

Given this clear evidence that those of skill in the art would recognize the present invention as a kinase, there can be no question that Applicants' asserted utility for the described sequences is "credible." Applicants have thus supplied evidence supporting their assertion that those of skill in the art would recognize that the sequences of the present invention encode a kinase. In contrast, the Examiner has provided no evidence of record indicating that those of skill in the art would not recognize the sequences of the present invention encode a kinase. As such, the scientific evidence clearly establishes that Applicants have described an invention whose utility is in full compliance with the provisions of 35 U.S.C. § 101, and the Examiner's rejection should be withdrawn.

IV. Rejections Under 35 U.S.C. § 112, First Paragraph

Claims 2-4 stand rejected under 35 USC section 112, first paragraph, as containing subject matter which allegedly was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected to make and/or use the invention. The Examiner alleges that because the claimed invention is not supported by either a specific asserted utility or a well established utility one skilled in the art clearly would not know how to use the claimed invention so that it would operate as intended without undue experimentation.

The Federal Circuit and its predecessor have determined that the utility requirement of Section 101 and the how to use requirement of Section 112, first paragraph, have the same basis - the disclosure of a credible utility. *See In re Brana*, 51 F.3d 1560, 1564, 34 USPQ2d 1436, 1441 (Fed. Cir. 1995); *see also In re Jolles*, 628 F.2d 1322, 1326 n.11, 206 USPQ 885, 889 n. 11 (CCPA 1980); and *In re Fouche*, 439 F.2d 1237, 1243, 169 USPQ 429, 434 (CCPA 1971). Applicants traverse this rejection on the ground that Claims 2-4 have been shown to have a specific, substantial, credible and well established utility have significant patentable utility as discussed in Section III, above. Applicants submit that when an Applicant satisfactorily rebuts a rejection based on a lack of utility under 35 U.S.C. § 101, the corresponding rejection imposed under 35 U.S.C. § 112, first paragraph, should also be withdrawn. Additionally, Applicants respectfully submit that, given the discussion provided above regarding well established utility and issued U.S. Patents 5,817,479 and 6,340,583 one of ordinary skill in the art would have clearly understood how to make and use the claimed invention, a novel human kinase, without undue experimentation. Applicants therefore respectfully request that the rejection of claims 2-4 under 35 U.S.C. § 112, first paragraph, be withdrawn.

V. Rejections Under 35 U.S.C. § 112, Second Paragraph

Claim 2 stands rejected under 35 USC section 112, second paragraph, as being allegedly indefinite, for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Although Applicants believe the claims as originally filed sufficiently point out and distinctly claim the invention, in order to more rapidly progress the case to allowance, Applicant's have amended Claim 2 .

Claim 2 stands rejected because the exact hybridization condition is allegedly unclear because the specification contains different stringent hybridization conditions. Although Applicants believe that this claim as originally filed sufficiently points out and distinctly claims the invention, in order to more rapidly progress the case to allowance, Applicants have amended Claim 2 to specify highly stringent conditions using the wash conditions defined in the specification verbatim. Applicants respectfully submit that this rejection has thus been overcome by Applicant's amendment of Claim 2. Accordingly, the Examiner is respectfully requested to withdraw the pending rejection of Claim 2 under 35 U.S.C. section 112, second paragraph.

VI. CONCLUSION

In view of the foregoing amendments and remarks, the Applicants believe that the application is in good and proper condition for allowance. Early notification to that effect is earnestly solicited.

If the Examiner feels that a telephone call would expedite the consideration of the application, the Examiner is invited to call the undersigned attorney at (281) 863-3333.

Respectfully submitted,

June 13, 2002
Date

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